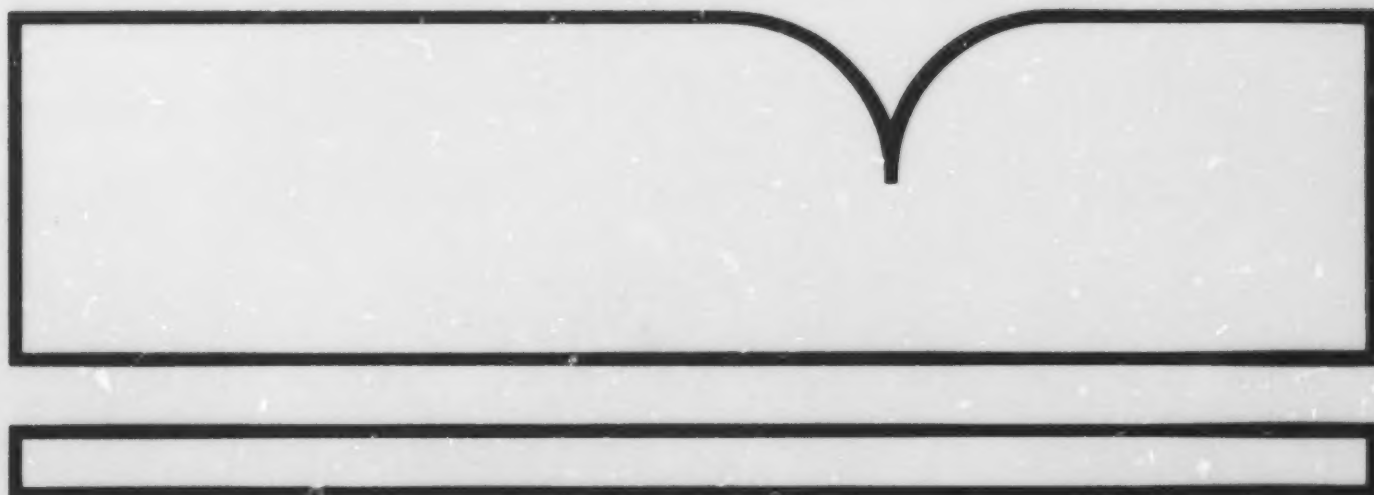


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Respiratory Responses of Vigorously
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Respiratory Responses of Vigorously Exercising Children to 0.12 ppm Ozone Exposure¹⁻⁴

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Introduction

Exercising children and adolescents may experience acute decrements in pulmonary function when exposed during normal activities to concentrations of ozone (O_3) at or below the present National Ambient Air Quality Standard of 0.12 part per million (ppm). In a study of children and young adults exercising under ambient conditions, Lebowitz and associates (1) observed a negative association between O_3 concentration and forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). These results suggested that such effects occur at concentrations below 0.12 ppm O_3 . Kagawa and coworkers (2, 3) studied 21 children 11 yr of age and reported that O_3 at concentrations as low as 0.10 ppm was associated with increased airways resistance (Raw). Fifty-eight children 8 to 13 yr of age at a summer camp were studied by Lippmann and associates (4), whose data suggested that decrements in pulmonary function occurred at O_3 concentrations below 0.12 ppm. Estimates of the ambient O_3 concentrations at the camp were imprecise, however, because the O_3 monitors were located 20 and 60 miles from the exposure site.

Controlled environmental chamber studies indicate that changes in respiratory function and symptoms occur in adults during exposure with heavy exercise to concentrations of O_3 at or above 0.12 ppm (5, 6), but not to lower concentrations. In a study of 135 heavily exercising young adults divided into 6 groups with each group exposed to either 0.0, 0.12, 0.18, 0.24, 0.30, or 0.40 ppm O_3 , McDonnell and coworkers (5) observed temporary reductions in FVC and forced expiratory flow rates and the induction of cough following exposure to 0.12 and 0.18 ppm O_3 . During exposure to 0.24, 0.30, and 0.40 ppm O_3 , subjects experienced larger changes in these variables and a decrease in tidal volume (V_T) and increases in respiratory frequency (f), specific airways resistance (SRaw), shortness

SUMMARY Changes in respiratory function have been suggested for children exposed to less than 0.12 ppm ozone (O_3) while engaged in normal activities. Because the results of these studies have been confounded by other variables, such as temperature or the presence of other pollutants or have been questioned as to the adequacy of exposure measurements, we determined the acute response of children exposed to 0.12 ppm O_3 in a controlled chamber environment. Twenty-three white males 8 to 11 yr of age were exposed once to clean air and once to 0.12 ppm O_3 in random order. Exposures were for 2.5 h and included 2 h of intermittent heavy exercise. Measures of forced expiratory volume in one second (FEV_1) and the symptom cough were determined prior to and after each exposure. A significant decline in FEV_1 was found after the O_3 exposure compared to the air exposure, and it appeared to persist for 16 to 20 h. No significant increase in cough was found due to O_3 exposure. Forced vital capacity, specific airways resistance, respiratory frequency, tidal volume, and other symptoms were measured in a secondary exploratory analysis of this study.

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of breath, and pain upon deep inspiration. There were no significant changes in these latter variables for the groups exposed to 0.12 or 0.18 ppm O_3 . Folinsbee and associates (6) exposed 10 heavily exercising young adults to 0.0, 0.10, 0.30, and 0.50 ppm O_3 . They observed no changes in respiratory function or symptoms due to the 0.10 ppm exposure. They did observe decreases in FVC, forced expiratory flow rates, and V_T , and increases in SRaw and f following exposure to 0.30 and 0.50 ppm O_3 . In a study of 50 young adult cyclists exercising heavily for 1 h, Avol and coworkers (7) observed similar changes in pulmonary function and symptoms for subjects exposed to 0.16 ppm, but not to 0.08 ppm O_3 . Controlled exposures of children under similar circumstances to those reported for adults have not been performed, nor are sufficient data available to adequately assess the response of children in these circumstances.

The purpose of this study was to determine the acute respiratory responses of children exposed to 0.12 ppm O_3 and to compare these responses to those previously measured in adults. Because we chose the lowest level of O_3 for which measurable effects had been demonstrated in adults, we expected changes to be small and only present in the most sensitive variables. For this reason, we limited our formal hypothesis testing

analyses to changes in FEV_1 and the symptom cough. The results of this study indicate that this level of exposure results in decrements in pulmonary function similar to those seen in adults, but without an increase in cough.

Methods

Subjects for this study were healthy white males, 8 to 11 yr of age ($n = 23$). None of the subjects had smoked or had asthma, al-

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lergic rhinitis, cardiac disease, chronic respiratory disease, recent acute respiratory illness, or extensive exposure to pollutants. They were recruited through newspaper advertisements directed toward parents. Prior to accepting volunteers we explained the study in detail to parents by telephone and mailed explanations of the study to prospective subjects and their parents.

At least 1 day prior to initiation of the exposure protocol, each subject and his parent(s) visited the laboratory and were informed again of the purposes, design, and procedures of the experiment, as well as the potential risk of participation. The subject and his parent(s) each signed consent forms. The subject's consent form was written at a level understandable for this age group. This study was approved by the Committee on the Protection of the Rights of Human Subjects of the University of North Carolina School of Medicine.

During the first visit to the laboratory, parents completed a pediatric health survey form and were interviewed by a pediatrician. Each subject had a physical examination and routine hematologic and blood chemistry tests performed. Subjects were trained in the techniques for obtaining plethysmographic and spirometric measurements. At this time they also exercised on a treadmill, and the speed and grade of incline required to produce a minute ventilation ($\dot{V}_E$) of approximately 35 L/min/m² body surface area (BSA) were determined.

Each subject was exposed on two occasions separated by at least 1 wk. One exposure was to 0.12 ppm O₃ and the other was to clean air. Subjects were randomly assigned to order of exposure, and 0.08 ppm O₃ was introduced into the chamber for 5 min on the air exposure day as a sham. Approximately 50% of the subjects were exposed from 9:30 A.M. until noon and the other half from 2 to 4:30 P.M. Each subject underwent his two exposures at the same time of day, removing the potential for possible diurnal variation in pulmonary function to account for measured changes due to O₃ exposure. Neither subjects nor investigators had knowledge of the exposure conditions. On the morning after each exposure, subjects returned for repeat pulmonary function testing in clean air. An investigator was present in the chamber at all times during training, exposure, and follow-up.

Exposures and measurements were conducted in a 4 × 6 × 3.2-m stainless steel chamber maintained at 22° C and 40% relative humidity. Ozone was generated by passing incoming air over ultraviolet lights. The concentration of O₃ in the chamber was continuously monitored by chemiluminescence detection using Bendix model 8002 analyzers (Roncuerte, WV), which were calibrated daily against an ultraviolet O₃ photometer (Dasibi model 1003AH, Glendale, CA). A detailed description of the chamber and the O₃ generating, delivery, monitoring, and control systems has been previously published (8, 9).

Immediately prior to each exposure, subjects performed pre-exposure spirometry and

TABLE 1
CHARACTERISTICS OF EXERCISING SUBJECTS*

	Air	Ozone
$\dot{V}_E$ (L/min)	38.2 ± 6.2	39.3 ± 7.4
$\dot{V}_E/BSA$ (L/min/m ²)	32.4 ± 3.3	33.3 ± 3.4
HR (beats/min)	158 ± 13	158 ± 15
TRSP (mph)	2.9 ± 0.2	2.9 ± 0.2
TREL (%)	15.0 ± 0.0	15.0 ± 0.0

Definition of abbreviations: $\dot{V}_E$ = minute ventilation; BSA = body surface area; HR = heart rate; TRSP = treadmill speed; TREL = treadmill elevation.

* Values are mean ± SD.

plethysmography in clean air. At the beginning of each 2.5-h exposure, subjects completed a symptom questionnaire. During the first 2 h of exposure, subjects performed 4 cycles of 15 min of rest and 15 min of treadmill exercise at the speed and grade of incline determined during the training session to result in a $\dot{V}_E$ of 35 L/min/m² BSA. Measurements of breathing pattern and heart rate were measured for the twelfth minute of each exercise period. Subjects breathed freely during the entire exposure except for 2 min during each exercise period when they wore a noseclip and breathed through a mouthpiece for measurements of breathing pattern. This generally resulted in oronasal breathing during exercise and nasal breathing during rest. Spirometric and plethysmographic measurements were again made at 5 min and 25 min, respectively, after the final exercise period. Another symptom questionnaire was completed 10 min after this last period of exercise. To confirm our impressions that any effects were rapidly reversed, spirometric measurements and assessment of symptoms were performed the morning after each exposure.

Spirometric measurements were derived from FVC maneuvers performed on a 12-L dry seal spirometer (CPI model 220; Cardio-Pulmonary Instruments, Houston, TX). Each maneuver was evaluated by the investigator according to the following criteria: (1) maximal effort by the subject, (2) proper technical performance of the maneuver, (3) rapid upstroke of the flow-volume curve, and (4) reproducibility of the effort independent portion of the flow-volume curve. Maneuvers not satisfying all of the above criteria were not analyzed. We attempted to obtain 3 acceptable, maximal effort maneuvers for each session with no more than 8 maneuvers performed. Forced expiratory volume in one second, expiratory flow rate between 25 and 75% FVC (FEF₂₅₋₇₅), and peak expiratory flow rate (PEF) were also calculated for each maneuver. For each session the single largest FVC, the single largest FEV₁, and the single largest PEF were selected for analysis. For each maneuver, the sum of FVC and FEV₁ was calculated and the FEF₂₅₋₇₅ from the maneuver with the largest sum was analyzed.

Airway resistance (Raw), thoracic gas volume (Vtg), and SRaw were determined with subjects seated in a standard variable-pressure body plethysmograph (CPI model 2000TB)

and panting at 1.5 Hz. Slopes of flow versus box pressure were measured at flows between -0.5 and +0.5 L/s. Four to 6 breaths were averaged for the calculation of each variable. Measurements were made in triplicate, although infrequently; fewer than 3 satisfactory measurements were obtained. Means of all satisfactory measurements are reported for each variable.

During exercise, $\dot{V}_E$, Vt, and f were obtained by digital integration of flow signals from a Fleisch no. 3 pneumotachometer (Lausanne, Switzerland). Tidal volume and $\dot{V}_E$ were corrected to body temperature pressure saturated. Using single-channel telemetry, heart rate and electrocardiogram (ECG) were continuously monitored throughout the exposure. Minute ventilation, f, Vt, and heart rate were measured during the eleventh and twelfth minutes of exercise, and running averages were calculated every 10 s. The means of these running averages for the twelfth minute were used for analysis.

The symptom questionnaires contained 3 questions regarding the presence and severity of cough, shortness of breath, and pain on deep inspiration. Subjects were asked to classify their response to each question as none, mild, moderate, or severe. For purposes of statistical analysis, a score of 1 was assigned to none, 2 to mild, 3 to moderate, and 4 to severe.

For pulmonary function variables and symptoms, differences between pre-exposure and final measurements were analyzed. For f and Vt during exercise, differences between measurements obtained during the first and fourth exercise periods were analyzed.

The two hypotheses to be formally tested in this analysis were whether the decrement in FEV₁ and the increment in presence and severity of cough following O₃ exposure were larger than those following air exposure. As exploratory analyses, changes in other measured variables known to be affected by higher level O₃ exposure of adults or by low level O₃ exposure of children in field studies were assessed in a similar manner. These were FVC, FEF₂₅₋₇₅, PEF, f, Vt, SRaw, pain upon deep inspiration, and shortness of breath. A further exploratory analysis compared FVC, FEV₁, FEF₂₅₋₇₅, PEF, and symptoms measured 1 day after O₃ exposure to those measured 1 day after air exposure. For all analyses performed in this study, data were analyzed both as absolute values and as percents of predicted values. The data presented are for the absolute values; however, the outcome of the two analyses were nearly identical. In all cases the one-tailed paired Student's *t* test was used to make these comparisons.

Results

Twenty-six children were interviewed for participation in this study. One child was excluded for an abnormal flow-volume curve, and 2 other children withdrew before testing began. All other children completed the study without difficulty,

TABLE 2
FORCED EXPIRATORY VOLUME IN ONE SECOND MEASURED DURING
AIR AND OZONE EXPOSURES

Subject	Air			Ozone		
	Pre	Post	Follow-up*	Pre	Post	Follow-up*
1	2,256	2,274	2,269	2,324	2,299	2,189
2	1,669	1,832	1,732	1,831	1,780	1,758
3	1,954	1,935	1,930	1,949	1,845	1,818
4	1,675	1,656	†	1,709	1,697	†
6	2,331	2,264	2,239	2,245	2,090	2,188
7	2,511	2,490	2,545	2,409	2,541	2,411
8	2,281	2,345	2,294	2,252	2,287	2,316
9	1,937	1,911	1,885	2,061	1,919	†
10	1,841	1,807	1,813	1,795	1,714	1,784
11	1,431	1,686	†	1,615	1,513	1,466
12	2,251	2,122	2,115	2,179	2,147	2,021
13	1,824	1,789	1,789	1,803	1,700	1,809
14	1,670	1,638	†	1,794	1,788	1,702
16	1,519	1,495	1,592	1,532	1,312	1,560
17	1,542	1,465	1,447	1,524	1,191	1,436
18	2,372	2,205	2,223	2,233	2,121	2,222
20	1,643	1,654	1,657	1,673	1,583	1,712
21	2,349	2,416	2,451	2,353	2,287	2,399
22	2,519	2,549	2,619	2,545	2,590	2,627
24	2,340	2,365	2,531	2,487	2,424	2,506
25	1,606	1,416	†	1,502	1,592	1,502
26	1,824	1,801	1,828	1,836	1,759	1,867
Mean	1,970	1,960	2,063‡	1,984	1,917	2,037‡
SD	356	355	367	335	385	350

* Follow-up measurements were made the morning after exposure.

† Missing data.

‡ These statistics only include subjects who completed both follow-up measurements ($n = 17$).

except that spirometric data for 1 subject were excluded from analysis because of his inability to reproducibly perform a technically satisfactory maneuver.

The level of exercise and ventilatory response to exercise were similar for all subjects during the air and O₃ exposures (table 1). Measures of lung function were also similar prior to both the air and O₃

exposures (tables 2 and 3). Pre-exposure FEV₁ measurements for the 2 exposure days differed by less than 5% of the larger value for all subjects except seven, and differed by less than 10% for all subjects except one.

Forced expiratory volume in one second was significantly decreased by 67 ± 21 ml (mean $\pm$ SE) during the O₃ ex-

posure, compared to a decrease of 10 ± 21 ml during the control exposure (tables 2 and 3). Frequency and severity of cough did not increase significantly in children exposed to O₃ compared to air (table 3).

For the exploratory analyses, a decrement in PEF following the O₃ exposure compared to the air exposure was observed at the $\alpha = 0.05$ level (table 3). Decrements in FVC and induction of shortness of breath and pain upon deep inspiration approached significance at this level. No significant changes were observed for FEF₂₅₋₇₅, SRaw, f, or Vt.

As part of the exploratory analysis, 17 of the subjects returned the day after each exposure to perform spirometric measurements and to complete the symptom questionnaire. On the day after O₃ exposure, FEV₁ was marginally depressed ($p = 0.035$) relative to the day after the air exposure (table 2). No other pulmonary function variables or symptoms were significantly changed 1 day after the O₃ exposure, although changes in FVC and FEF₂₅₋₇₅ were mildly suggestive ($p = 0.20$ and 0.13 , respectively).

Discussion

In order to ensure that rejection of a null hypothesis was not due simply to testing multiple hypotheses, we limited the primary hypotheses tested to changes in FEV₁ and cough. These variables were chosen because they demonstrated the most statistically significant changes seen in adults exposed under similar conditions to 0.12 ppm O₃ (5). We did, how-

TABLE 3
MEASURES OF RESPIRATORY FUNCTION BEFORE AND AFTER EXPOSURE*

	Air		Ozone		Difference†	
	Pre	Post-Pre	Pre	Post-Pre	Ozone-Air	p
Primary Analyses						
FEV ₁ ‡ (ml)	1,970 $\pm$ 76	-10 $\pm$ 21	1,984 $\pm$ 71	-67 $\pm$ 21	-56 $\pm$ 29	0.03
Cough§	1.1 $\pm$ 0.1	0.0 $\pm$ 0.1	1.1 $\pm$ 0.1	0.1 $\pm$ 0.2	0.1 $\pm$ 0.1	0.16
Secondary Exploratory Analyses						
FVC‡ (ml)	2,354 $\pm$ 82	-2 $\pm$ 16	2,341 $\pm$ 78	-42 $\pm$ 17	-40 $\pm$ 27	0.08
FEF ₂₅₋₇₅ ‡ (L/s)	2.13 $\pm$ 0.14	-0.05 $\pm$ 0.04	2.18 $\pm$ 0.13	-0.12 $\pm$ 0.05	-0.07 $\pm$ 0.08	0.19
PEF‡ (L/s)	4.43 $\pm$ 0.17	0.10 $\pm$ 0.09	4.58 $\pm$ 0.17	-0.12 $\pm$ 0.09	-0.22 $\pm$ 0.13	0.05
SRaw† (cm·s)	4.64 $\pm$ 0.36	-0.33 $\pm$ 0.15	4.58 $\pm$ 0.31	-0.09 $\pm$ 0.19	0.24 $\pm$ 0.22	0.15
f ** (min ⁻¹)	48 $\pm$ 1.9	2.7 $\pm$ 2.1	48 $\pm$ 2.0	2.0 $\pm$ 1.3	-0.7 $\pm$ 2.5	0.61
Vt†** (ml)	804 $\pm$ 28	-31 $\pm$ 19	840 $\pm$ 39	-48 $\pm$ 22	-16 $\pm$ 32	0.31
PDI§	1.0 $\pm$ 0.0	0.1 $\pm$ 0.1	1.1 $\pm$ 0.1	0.3 $\pm$ 0.2	0.2 $\pm$ 0.2	0.09
SB§	1.0 $\pm$ 0.0	0.0 $\pm$ 0.0	1.0 $\pm$ 0.0	0.3 $\pm$ 0.2	0.2 $\pm$ 0.2	0.09

Definition of abbreviations: FEV₁ = forced expiratory volume in one second; FVC = forced vital capacity; FEF₂₅₋₇₅ = mean expiratory flow rate between 25 and 75% of FVC; PEF = peak expiratory flow rate; SRaw = specific airway resistance; f = respiratory rate; Vt = tidal volume; PDI = pain on deep inspiration; SB = shortness of breath.

* Values are mean $\pm$ SE.

† This is the difference of the pre-post differences for the ozone and air exposures. p tests the null hypothesis that this difference equals zero.

‡ $n = 22$.

§ $n = 21$.

|| Scores are none = 1, mild = 2, moderate = 3, severe = 4.

** $n = 23$.

Pre- and post-measurements were actually taken during the first and fourth exercise periods, respectively, during exposure.

ever, measure other respiratory function and symptom variables and have reported these as exploratory analyses. It must be noted that the results of these exploratory analyses cannot be interpreted as tests of hypotheses, but must be considered descriptive. It must also be noted that inferences drawn from this study can only be applied to heavily exercising children. Resting or lightly exercising children would have much smaller minute ventilations than our subjects and would be breathing primarily by the nasal route, whereas our subjects were primarily breathing oronasally during exercise and nasally during rest. This would result in a smaller dose of O_3 to the lower airways, and probably no measurable changes in lung function during resting exposure to 0.12 ppm O_3 would be observed. However, because our subjects were exposed without the encumbrance of facemasks, noseclips, or mouthpieces except for 8 min during measurements, we believe this exposure is representative of the type of O_3 exposure active children would experience under ambient conditions.

The results of this study indicate that exposure of children to 0.12 ppm O_3 results in small decrements in $FEV_{1.0}$, and exploratory analyses suggest that there may also be decrements in FVC and in forced expiratory flow rates. The pattern of results found here is similar to that reported by other authors (5, 6) who found simultaneous decrements in FVC, $FEV_{1.0}$, and FEF_{25-75} . These changes are consistent with the prevailing hypothesis that O_3 produces a primary decrease in the ability to inhale maximally, which necessarily results in decrements in forced expiratory flows. The relative magnitude of the mean decrements as a percentage of baseline is similar to that reported by McDonnell and coworkers (5) in a study of 6 groups of 18 to 30-yr-old nonsmoking males. Those subjects underwent 2.5-h exposures with 2 h of intermittent heavy treadmill exercise at an average speed of 3.6 miles per hour and an 11.6% grade of incline. This was sufficient to produce a $\dot{V}_E$ of 35 L/min/m² BSA ($\dot{V}_E = 67$ L/min) and a heart rate of 164 beats per minute. One group of 20 subjects was exposed to clean air and another group of 22 subjects was exposed to 0.12 ppm O_3 . The air group had decrements in FVC, $FEV_{1.0}$, and FEF_{25-75} of 1, 1, and 0%, and the 0.12 ppm O_3 group had significantly greater decrements of 3, 5, and 7%, respectively. These decrements are comparable to the ones reported here of 0, 1, and 2% for air, and 2, 3, and 6% for O_3 . No differences between air and O_3

exposures were measured for changes in $SRaw$, f , or V_T for either study. These data indicate that, as a percent of baseline, the mean magnitude of decrements in pulmonary function due to O_3 exposure are similar in children and adults.

In contrast to the results seen in adults (5), children did not appear to develop symptoms of cough during this exposure. Although one possible explanation for this is that children are less likely to remember and report symptoms than are adults, qualitative observation by the investigators suggest that only rarely did children cough during any exposure, even when inhaling maximally for pulmonary function testing. This suggests that O_3 may induce cough to a greater extent in adults than in children. The reasons for this observed difference are not clear. The absence of cough in children following this O_3 exposure is not due to a generalized lack of a cough response, as children cough vigorously in response to foreign bodies and during and following upper respiratory infections. Children with asthma frequently have an otherwise unexplained cough. It is unlikely that the difference between adults and children is due to any difference in the quantity of mucus produced, as the cough associated with O_3 exposure is usually non-productive (10, 11). It has been hypothesized that O_3 produces cough and changes in lung function by stimulation of afferent airway receptors either directly or indirectly by causing epithelial cell damage, the release of mediators, or through chemical intermediates due to reactions of O_3 with airway surface liquid (5). Observations by Sheppard and associates (12) indicate that the airway receptors responsible for changes in cough following inhalation of distilled water by asthmatics are distinct from those responsible for changes in pulmonary function either in location or in sensitivity to inhaled lidocaine. Eschenbacher and coworkers (13) demonstrated that changes in cough and bronchoconstriction can be independently produced by use of two different stimuli, and therefore, that the pathways are distinct for these two responses. We can only speculate that some step in the pathways responsible for producing cough due to O_3 exposure in children is less sensitive than the corresponding one in adults, while the pathways responsible for changes in lung function are of similar sensitivity to O_3 or its by-products.

The finding of a slightly depressed $FEV_{1.0}$ the day after O_3 exposure compared to the day after air exposure was unex-

pected (table 2). Due to the number of exploratory hypotheses generated, and a p value of 0.035, it is possible that this observation occurred by chance alone. It does, however, raise the question of how quickly these responses resolve. Previous studies of adults recurrently exposed to levels of O_3 sufficient to produce acute decrements in $FEV_{1.0}$ have provided no conclusive evidence about residual effects. In one study of lightly exercising adults exposed to clean air on 1 day and 0.42 ppm O_3 on the next 4 days, there was a significant decline in baseline FVC and $FEV_{1.0}$ during the 5 days. Interpretation is difficult, however, because part of that decline occurred on the day after clean air exposure (14). In another study of adults exposed to 0.40 ppm by Farrell and associates (15), FVC tended to decline slightly over 5 days, although no tests of significance were reported. In contrast to these findings, Hackney and coworkers (16) and Folinsbee and associates (17) exposed subjects to O_3 on 4 successive days and observed no decline in baseline FVC or $FEV_{1.0}$ during the 4 days.

To assess the duration of the apparent residual effect observed in this study, we compared values of $FEV_{1.0}$ measured 1 wk after exposure with those measured prior to exposure. Because no subjects had measurements made 1 wk after their second exposures, the group was divided into two subgroups, one having first been exposed to O_3 ($n = 12$) and the other having first been exposed to air ($n = 10$). The baseline measurements for the second exposure were used as the 1-wk follow-up for the first exposure. For the twelve subjects first exposed to O_3 , pre-exposure $FEV_{1.0}$ on that day was 1,975 ml. One week later, prior to their air exposure, these same subjects had a baseline $FEV_{1.0}$ of 1,923 ml. The difference of 52 ± 23 ml (mean $\pm$ SE) represents a 1-wk follow-up to the O_3 exposure. For the 10 subjects first exposed to clean air, pre-exposure $FEV_{1.0}$ on the air exposure day was 2,027 ml and 1 wk later on the O_3 exposure day was 1,995 ml. The difference of 32 ± 16 ml represents the 1-wk follow-up to an air exposure. The differences between the O_3 exposed first group and the air exposed first group were not significantly different ($p = 0.29$) by the one-tailed unpaired Student's t test. This indicates that we were unable to detect a significant residual effect of O_3 exposure 1 wk after the exposure.

Because performance of forced expiratory spirometry by children of this age group may be less reproducible than for

adults, we carefully screened all flow volume curves according to criteria outlined in METHODS, and we have presented the individual data for both exposures (table 2). Responses were remarkably reproducible from day to day with few exceptions. In 95% of the subjects, the smaller of the 2 baseline values was within 10% of the larger, and in 68% of the subjects was within 5%. The mean absolute difference between the two baseline measurements was 3.6% of the larger value. The reported analyses were conducted on all available data. Examination of the individual data reveals that baseline values for Subjects 2 and 11 were quite variable, and that Subject 25 had a greater than 10% decrement in the clean air exposure. These are probably chance occurrences and have no physiologic significance. Reanalysis of the data excluding these 3 subjects resulted in a small decrease in the p value for FEV₁, with no change in the interpretation of the results.

In summary, we have observed that exposure of 8 to 11-yr-old boys to 0.12 ppm for 2 h during heavy intermittent exercise results in small decrements in FEV₁ without induction of cough. The magnitude of the FEV₁ change is consistent with that demonstrated under similar exposure conditions in adults. Furthermore, there is a suggestion that small decrements in FEV₁ may persist for 16 to 20 h after O₃ exposure. The failure of O₃ to induce cough in children is in contrast to results reported for adults.

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